**Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (canceled)

2. (previously presented) The method of claim 6, wherein the marker that reflects the activity of osteoblasts is:

(1) a marker associated with the phase of osteoblast proliferation and matrix formation and a marker associated with the phase of calcification; or

(2) a marker associated with the phase of matrix maturation and a marker associated with the phase of calcification.

3. (previously presented) The method according to claim 6, wherein the marker that reflects the activity of osteoblasts is:

(1) Carboxyterminal propeptide of type I procollagen or Amino terminal propeptide of type I procollagen and osteocalcin; or

(2) Bone specific alkaliphosphatase and osteocalcin.

4. (currently amended) The method according to claim 6, wherein the marker that reflects the ~~action~~ activity of osteoclasts is a marker associated with bone type I collagen.

5. (currently amended) The method according to claim 6, wherein the marker that reflects the ~~action~~ activity of osteoclasts is deoxypyridinoline and/or Carboxyterminal telopeptide of type I collagen.

6. (currently amended) In a ~~A~~ method of diagnosing amelioration and/or exacerbation of metastasis of malignant tumor to bone in a patient with a cancer disease,

using markers that reflect the activity of osteoblasts and markers that reflect the ~~action~~ activity of osteoclasts,

1) wherein the markers that reflect the activity of osteoblasts are

a) ~~one or more markers~~ a marker associated with the phase of calcification, and

b) ~~one or more markers~~ a marker associated with the phase of osteoblasts proliferation and/or matrix formation,

2) wherein the ~~one or more markers~~ marker that ~~reflect~~ reflects the activity of osteoclasts ~~are markers~~ is a

marker associated with osteoclasts targeted to evaluation of worsening of the disease,

comprising testing blood from said patient for a marker of bone metabolism,

wherein the amelioration of bone metastasis or therapeutic effect and the degree of the exacerbation of bone metastasis are diagnosed by monitoring said markers,

the improvement wherein said testing comprises measuring for both osteocalcin and one marker selected from BALP, PICP and PINP,

determining a Z value for each of said osteocalcin and said marker, each said Z value being determined by dividing the difference between said measured value for said patient and an average value for patients with bone metastasis, by a standard deviation of a patient without bone metastasis, and determining a crossover index by dividing said Z value for osteocalcin by said Z value for BALP, PICP or PINP,

said crossover index providing a diagnosis of progression of bone metastasis in the treatment of said patient for said cancer.

7. (Canceled)

8. (currently amended) In a ~~A~~ method of evaluating the efficacy of drugs for treatment of a cancer disease,

using ~~one or more~~ a formative ~~markers~~ marker that reflects the activity of osteoblasts ~~and one or more~~ or a ~~resorptive markers~~ marker that ~~reflect~~ reflects the activity of osteoclasts,

1) wherein the markers that reflect the activity of osteoblasts are

a) ~~one or more markers~~ a marker associated with the phase of calcification, and

b) ~~one or more markers~~ a marker associated with the phase of osteoblasts proliferation and/or matrix formation,

2) wherein the ~~one or more markers~~ marker that ~~reflect~~ reflects the activity of osteoclasts ~~are markers~~ is a marker associated with osteoclasts targeted to evaluation of worsening of the disease,

comprising testing blood from said patient for a marker of bone metabolism,

wherein the amelioration of bone metastasis or therapeutic effect and the degree of the exacerbation of bone metastasis are diagnosed correctly by monitoring said markers

the improvement wherein said testing comprises measuring for both osteocalcin and one marker selected from BALP, PICP and PINP,

determining a Z value for each of said osteocalcin and said BALP, each said Z value being determined by dividing the difference between said measured value for said patient and an average value for patients with bone metastasis, by a standard deviation of a patient without bone metastasis, and determining a crossover index by dividing said Z value for osteocalcin by said Z value for BALP, PICP or PINP,

said crossover index providing a diagnosis of progression of bone metastasis and evaluation of drug efficacy in the treatment of said patient for said cancer.

9. (currently amended) The method according to claim 8, wherein the drug evaluated is a cancer control therapeutic agent.

10. (currently amended) The method according to claim 8, wherein the drug evaluated is a bone resorption suppressant.

11. (currently amended) The method according to claim 8, wherein the drug evaluated is an endocrine therapeutic agent.

12. (previously presented) The method according to claim 8, wherein the marker that reflects the activity of osteoblasts is:

(1) a marker associated with the phase of osteoblast proliferation and matrix formation and a marker associated with the phase of calcification; or

(2) a marker associated with the phase of matrix maturation and a marker associated with the phase of calcification.

13. (previously presented) The method according to claim 8, wherein the marker that reflects the activity of osteoblasts is:

(1) Carboxyterminal propeptide of type I procollagen or Amino terminal propeptide of type I procollagen and osteocalcin; or

(2) Bone specific alkaliphosphatase and osteocalcin.

14. (currently amended) The method according to claim 8, wherein the marker that reflects the ~~action~~ activity of osteoclasts is a marker associated with bone type I collagen.

15. (currently amended) The method according to claim 8, wherein the marker that reflects the ~~action~~ activity

of osteoclasts is deoxypyridinoline and/or Carboxyterminal telopeptide of type I collagen.

Claims 16-24 (Cancelled).

25. (New) The method according to claim 6 or 8, wherein said cancer disease is prostate cancer.

26. (New) The method according to claim 6 or 8, wherein said cancer disease is breast cancer.

27. (New) The method according to claim 8, wherein the drug evaluated is a cancer control therapeutic agent.

28. (New) The method according to claim 8, wherein the drug evaluated is a bone resorption suppressant.

29. (New) The method according to claim 8, wherein the drug evaluated is an endocrine therapeutic agent.

30. (New) In a method of evaluating the efficacy of a drug for the treatment of cancer or for the inhibition or amelioration of a metastasis of said cancer to bone in a patient with cancer, wherein said cancer is selected from the group consisting of prostate cancer and breast cancer,

the improvement wherein said testing comprises measuring for both osteocalcin and for BALP, PICP or PINP,

determining a Z value for each of said osteocalcin and said BALP, PICP or PINP, each said Z value being determined by dividing the difference between said measured value for said patient and an average value for patients with bone metastasis, by a standard deviation of a patient without bone metastasis, and determining a crossover index by dividing said Z value for osteocalcin by said Z value for BALP, PICP or PINP,

said crossover index providing a diagnosis of progression of bone metastasis and evaluation of drug efficacy in the treatment of said patient for said cancer.